

Association Between Fine Particulate Matter and Oxidative DNA Damage May Be Modified in Potentially Susceptible Populations



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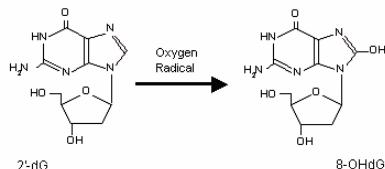


Introduction

- Fine particulate matter ($PM_{2.5}$) is a complex mixture of compounds, including polycyclic aromatic hydrocarbons and transition metals, that have been shown to induce oxidative DNA damage through the production of reactive oxygen species.
- Oxidative DNA damage induced by $PM_{2.5}$ exposure potentially may initiate carcinogenesis and serve as a marker of oxidative stress relevant for other adverse health outcomes such as hypertension, asthma or other cardiopulmonary diseases.
- Oxidative DNA damage and repair can be assessed using urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) as a biomarker.

8-hydroxy-2'-deoxyguanosine (8-OHdG)

- Particular type of ROS-induced DNA base modification.
- Repair mechanism after 8-OHdG is incorporated into DNA involves base and nucleotide excision with DNA-specific nucleosides excreted into urine.



8-OHdG Formation by Oxidative Stress

From H. Kasai, Environmental Mutagen Research 10:73-78, 1998

Study Objective

- To investigate the association between personal exposure to $PM_{2.5}$ and urinary 8-OHdG levels.
- Hypothesis I: Exposure to $PM_{2.5}$ is associated with oxidative DNA damage, as indicated by increased urinary 8-OHdG levels.
- Hypothesis II: Pre-existing cardiopulmonary diseases such as high blood pressure and asthma modify the effect of $PM_{2.5}$ on oxidative DNA damage.

Study Population and Design

- Community-based inner-city population living in close proximity to a bus terminal (one of the busiest Massachusetts Bay Transportation Authority bus stops in Boston) and a busy urban intersection.
- Study population recruited from Upham's Corner Health Center. Hypertensive and asthmatic subjects identified as those self-reporting physician-diagnoses.
- Prospective, repeated-measures design assessing urinary 8-OHdG levels in relation to personal exposure to $PM_{2.5}$ over a 36-hour period.

Methods

- Questionnaire data: medical, smoking, and work history.
- Continuous personal $PM_{2.5}$ monitoring over a 36-hr period using TSI SIDEPAK AM510 Personal Aerosol Monitor.
- Urine samples collected at baseline and at 12-hr intervals. 8-OHdG levels measured using ELISA and creatinine adjusted.



TSI SIDEPAK AM510
From www.tsi.com

Statistical Analysis

- Analysis using linear mixed models (compound symmetry covariance structure).
- Change in urinary 8-OHdG levels (Δ 8-OHdG) regressed on log-transformed $PM_{2.5}$ for each 12-hr interval ($\ln PM_{2.5}$).
- An interaction term between $\ln PM_{2.5}$ and dichotomized hypertension or asthma status included.
- Confounding by age, gender, and smoking status also examined.

Results

Study Demographics

Total # of subjects	20
Gender	
Males	4
Females	16
Race	
White	1
Black	7
Hispanic	5
Capeverdian	7
Mean age, yrs (range)	44 (21-69)
# of current smokers (%)	6 (30%)
# with hypertension (%)	11 (55%)
# on medication (%)	9 (45%)
# with asthma (%)	7 (35%)

Outcome and Exposure Assessment

	Mean	Median	Range
Urinary 8-OHdG (n = 74), $\mu\text{g/g}$ creatinine	11.1	10.5	(0.9, 26.3)
12-h avg $PM_{2.5}$ adj*** (n = 52), $\mu\text{g/m}^3$	30.2	18.1	(3.7, 261.9)

* Comparisons with gravimetric measurements indicated that SIDEPAK overestimated $PM_{2.5}$ concentrations. A correction factor of 0.45 for smokers and 0.29 for nonsmokers applied.

** 12-h avg $PM_{2.5}$ concentrations found to be log-normally distributed (geometric mean: 19.3 $\mu\text{g/m}^3$).

Linear Mixed Model Analyses

	β (95% CI)
Univariate model: $\ln PM_{2.5}$	-1.51 (-2.92, -0.09)
Hypertension model: $\ln PM_{2.5}$ hypertension	2.15 (-1.24, 5.53) 10.40 (-0.81, 21.61)
	-4.14 (-7.86, -0.42)
Asthma model: $\ln PM_{2.5}$ asthma	-1.93 (-3.31, -0.55) -13.99 (-29.01, 1.03)
	4.70 (-2.01, 9.60)

* Age, gender, smoking status not found to confound/modify association between Δ 8-OHdG and $\ln PM_{2.5}$.

Conclusions

- Association between $PM_{2.5}$ exposure and urinary 8-OHdG levels may be modified by preexisting cardiopulmonary diseases such as hypertension and asthma.
- $PM_{2.5}$ -related increases in urinary 8-OHdG in asthmatics compared to non-asthmatics suggest that asthmatics may be more susceptible to oxidative DNA damage from $PM_{2.5}$ exposure.
- Decreased $PM_{2.5}$ -related changes in urinary 8-OHdG in individuals with hypertension may be due to use of antihypertensive medication, some of which have been shown to have antioxidant properties.



* This poster has been reviewed by the National Center for Environmental Assessment, U.S. Environmental Protection Agency, and approved for presentation. Approval does not signify that the contents necessarily reflect the views and policies of the Agency.